Molecular Imaging for Stem Cell Science and Clinical Application

Grant Award Details

Molecular Imaging for Stem Cell Science and Clinical Application

Grant Type: Research Leadership

Grant Number: LA1-06919

Project Objective: Accelerating the development of stem cell therapies with non-invasive cell tracking through two tracks: 1)MRI technology development for imaging stem cells a) MRI reporters b) visualize stem cell viability c)inflammation and stem cells 2) Develop molecular imaging center at the Sanford Consortium for Regenerative Medicine (SCRM)

Investigator:

Name:	Eric Ahrens
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Amyotrophic Lateral Sclerosis, Neurological Disorders, Spinal Cord Injury

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: $5,920,899

Status: Active

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Molecular Imaging for Stem Cell Science and Clinical Application

Public Abstract: Stem cells offer tremendous potential to treat previously intractable diseases. The clinical translation of these therapies, however, presents unique challenges. One challenge is the absence of robust methods to monitor cell location and fate after delivery to the body. The delivery and biological distribution of stem cells over time can be much less predictable compared to conventional therapeutics, such as small-molecule therapeutic drugs. This basic fact can cause road blocks in the clinical translation, or in the regulatory path, which may cause delays in getting promising treatments into patients. My research aims to meet these challenges by developing new non-invasive cell tracking platforms for emerging stem cell therapies. Recent progress in magnetic resonance imaging (MRI) has demonstrated the feasibility of non-invasive monitoring of transplanted cells in patients. This project will build on these developments by creating next-generation cell tracking technologies with improved detectability and functionality. Additionally, I will provide leadership in the integration of non-invasive cell tracking into stem cell clinical trials. Specifically, this project will follow three parallel tracks. (1) The first track leverages molecular genetics to develop new nucleic acid-based MRI reporters. These reporters provide instructions to program a cell's innate machinery so that they produce special proteins with magnetic properties that impart MRI contrast to cells, and allow the cells to be seen. My team will create neural stem cell lines with MRI reporters integrated into their genome so that those neural stem cell lines, and their daughter cells, can be tracked days and months after transfer into a patient. (2) The second track will develop methods to detect stem cell viability in vivo using perfluorocarbon-based biosensors that can measure a stem cell's intracellular oxygen level. This technology can potentially be used to measure stem cell engraftment success, to see if the new cells are joining up with the other cells where they are placed. (3) The third project involves investigating the role that the host's inflammatory response plays in stem cell engraftment. These studies will employ novel perfluorocarbon imaging probes that enable MRI visualization and quantification of places in the body where inflammation is occurring. Overall, MRI cell tracking methods will be applied to new stem cell therapies for amyotrophic lateral sclerosis, spinal cord injury, and other disease states, in collaboration with CIRM-funded investigators.

Statement of Benefit to California:	California leads the nation in supporting stem cell research with the aim of finding cures for major diseases afflicting large segments of the state's population. Significant resources are invested in the design of novel cellular therapeutic strategies and associated clinical trials. To accelerate the clinical translation of these potentially live saving therapies, many physicians need method to image the behavior and movement of cells non-invasively following transplant into patients. My research aims to meet these challenges by developing new cell tracking imaging platforms for emerging stem cell therapies. Recent progress in magnetic resonance imaging (MRI) has demonstrated the feasibility of non-invasive monitoring of transplanted cells in patients. This project will build on these developments by leading the integration of MRI cell tracking into stem cell clinical trials and by developing next-generation technologies with improved sensitivity and functionality. Initially, MRI cell tracking methods will be applied to new stem cell therapies for amyotrophic lateral sclerosis and spinal cord injury. In vivo MRI cell tracking can accelerate the process of deciding whether to continue at the preclinical and early clinical trial stages, and can facilitate smaller, less costly trials by enrolling smaller patient numbers. Imaging can potentially yield data about stem cell engraftment success. Moreover, MRI cell tracking can help improve safety profiling and can potentially lower regulatory barriers by verifying survival and location of transplanted cells. Overall, in vivo MRI cell tracking can help maximize the impact of the State's investment in stem cell therapies by speeding-up clinical translation into patients. These endeavors are intrinsically collaborative and multidisciplinary. My project will create a new Stem Cell Imaging Center (SCIC) in California with a comprehensive set of ways to elucidate anatomical, functional, and molecular behavior of stem cells in model systems. The SCIC will provide scientific leadership to stem cell researchers and clinicians in the region, including a large number of CIRM-funded investigators who wish to bring state-of-the-art imaging into their clinical development programs. Importantly, the SCIC will focus intellectual talent on biological imaging for the state and the country. This project will help make MRI cell tracking more widespread clinically and position California to take a leadership role in driving this technology. An extensive infrastructure of MRI scanners already exist in California, and these advanced MRI methods would use this medical infrastructure better to advance stem cell therapies. Moreover, this project will lead to innovative new MRI tools and pharmaceutical imaging agents, thus providing economic benefits to California via the formation of new commercial products, industrial enterprises, and jobs.

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